

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Original) Pharmaceutical compositions comprising one or several agents as compound I which modulate the biological function of one or several of the VEGF/VEGF receptor systems, and comprising one or several agents as compound II which modulate the biological function of one or several of the Angiopoietin/Tie receptor systems.

2. (Original) Pharmaceutical compositions comprising one or several agents as compound I which are targeted to the endothelium via one or several of the VEGF/VEGF receptor systems, and comprising one or several agents as compound II which modulate the biological function of one or several of the Angiopoietin/Tie receptor systems.

3. (Original) Pharmaceutical compositions comprising one or several agents as compound I which modulates the biological function of one or several of the VEGF/VEGF receptor systems or of one or several of the Angiopoietin/Tie receptor systems and comprising one or several agents as compound II which are targeted to the endothelium.

4. (Original) Pharmaceutical compositions comprising one or several agents as compound I which modulate the biological function of one or several of the VEGF/VEGF receptor systems, and comprising one or several agents as compound II which are targeted to the endothelium via one or several of the Angiopoietin/Tie receptor systems.

5. (Original) Pharmaceutical compositions comprising one or several agents as compound I which are targeted to the endothelium via one or several of the VEGF/VEGF receptor systems, and comprising one or several agents as compound II which are targeted to the endothelium via one or several of the Angiopoietin/Tie receptor systems.

6. (Original) Pharmaceutical compositions comprising one or several agents as compound I which modulate the biological function of one or several of the VEGF/VEGF receptor systems, and comprising one or several agents as compound II which are targeted to the endothelium via one or several of the VEGF/VEGF receptor systems.

7. (Original) Pharmaceutical compositions comprising one or several agents as compound I which modulate the biological function of one or several of the Angiopoietin/Tie receptor systems, and comprising one or several agents as compound II which are targeted to the endothelium via one or several of the Angiopoietin/Tie receptor systems.

8. (Original) Pharmaceutical compositions comprising one or several agents which interfere with both the function of one or several of the VEGF/VEGF receptor systems and the function of one or several of the Angiopoietin/Tie receptor systems.

9. (Currently Amended) Pharmaceutical compositions according to ~~claims~~ claim 1-8 which are intended for simultaneous or separate sequential therapeutical application.

10. (Currently Amended) Pharmaceutical compositions according to ~~claims~~ claim 1-8 which comprise as compound I at least one of

- a) compounds which inhibit receptor tyrosine kinase activity,
- b) compounds which inhibit ligand binding to receptors,
- c) compounds which inhibit activation of intracellular signal pathways of the receptors,
- d) compounds which inhibit or activate expression of a ligand or of a receptor of the VEGF or Tie receptor system,
- e) delivery systems, such as antibodies, ligands, high-affinity binding oligonucleotides or oligopeptides, or liposomes, which target cytotoxic agents or coagulation-inducing agents to the endothelium via recognition of VEGF/VEGF receptor or Angiopoietin/Tie receptor systems,

delivery systems, such as antibodies, ligands, high-affinity binding oligonucleotides or oligopeptides, or liposomes, which are targeted to the endothelium and induce necrosis or apoptosis.

11. (Currently Amended) Pharmaceutical compositions according to ~~claims~~ claim 1-8 which comprise as compound II at least one of

- f) compounds which inhibit receptor tyrosine kinase activity,
- g) compounds which inhibit ligand binding to receptors,
- h) compounds which inhibit activation of intracellular signal pathways of the receptors,
- i) compounds which inhibit or activate expression of a ligand or of a receptor of the VEGF or Tie receptor system,
- j) delivery systems, such as antibodies, ligands, high-affinity binding oligonucleotides or oligopeptides, or liposomes, which target cytotoxic agents or coagulation-inducing agents to the endothelium via recognition of VEGF/VEGF receptor or Angiopoietin/Tie receptor systems,

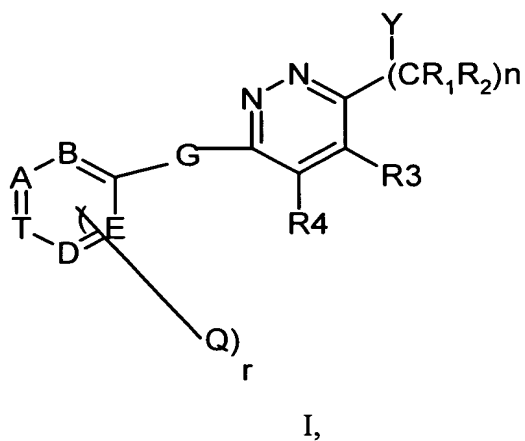
delivery systems, such as antibodies, ligands, high-affinity binding oligonucleotides or oligopeptides, or liposomes, which are targeted to the endothelium and induce necrosis or apoptosis.

12. (Currently Amended) Pharmaceutical compositions according to ~~claims~~ claim 1-44 which comprise as compound I and/ or II at least one of Seq. ID Nos. 1-59.

13. (Currently Amended) Pharmaceutical compositions according to claim 1 which comprise as compound I and/or II ~~Seq ID Nos.34a-~~ SEQ ID NO:60.

14. (Currently Amended) Pharmaceutical compositions according to ~~claims~~ claim 1-44 which comprise as compound I and/ or II at least one of sTie2, mAB 4301-42-35, scFv-tTF and/ or L19 scFv-tTFconjugate.

15. (Currently Amended) Pharmaceutical compositions according to ~~claims~~ claim 1-
~~44~~ which comprise as compound I and/ or II at least one small molecule of general formula I



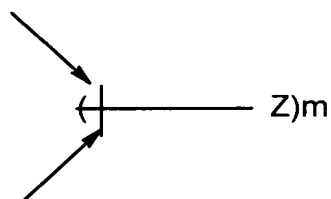
in which

r has the meaning of 0 to 2,

n has the meaning of 0 to 2;

R₃ und R₄ a) each independently from ~~each~~ each other have the
 meaning of lower alkyl,
 b) together form a bridge of general partial formula

II,



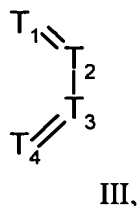
II,

wherein the binding is via the two terminal C- atoms,

and

m has the meaning of 0 to 4; or

c) together form a bridge of partial formula III



wherein one or two of the ring members T_1, T_2, T_3, T_4 has the meaning of nitrogen, and each others have the meaning of CH, and the ~~binding~~ binding is via the atoms T_1 and T_4 ;

G has the meaning of $C_1 - C_6$ - alkyl, $C_2 - C_6$ - alkylene or $C_2 - C_6$ - alkenylene; or $C_2 - C_6$ - alkylene or $C_3 - C_6$ - alkenylene, which are substituted with acyloxy or hydroxy; $-CH_2-O-$, $-CH_2-S-$, $-CH_2-NH-$, $-CH_2-O-CH_2-$, $-CH_2-S-CH_2-$, $-CH_2-NH-CH_2$, oxa (-O-), thia (-S-) or imino (-NH-),

A, B, D, E and T independently from each other have the meaning of N or CH, with the provisio that not more than three of these Substituents have the meaning of N,

Q has the meaning of lower alkyl, lower alkyloxy or halogene,

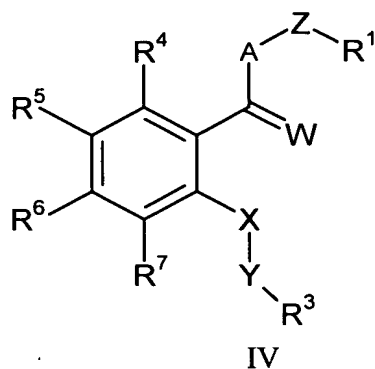
R_1 and R_2 independently from each other have the meaning of H or lower alkyl,

X has the meaning of imino, oxa or thia;
 Y has the meaning of hydrogen, unsubstituted or substituted aryl, heteroaryl, or unsubstituted or substituted cycloalkyl; and

Z has the meaning of amino, mono- or disubstituted amino, halogen, alkyl, substituted alkyl, hydroxy, etherificated or esterificated hydroxy, nitro, cyano, carboxy, esterificated carboxy, alkanoyl, carbamoyl, N-mono- or N, N- disubstituted carbamoyl, amidino, guanidino, mercapto, sulfo, phenylthio, phenyl-lower-alkyl-thio, alkyl-phenyl-thio, phenylsulfinyl, phenyl-lower-alkyl-sulfinyl, alkylphenylsulfinyl, phenylsulfonyl, phenyl-lower-alkan-sulfonyl, or alkylphenylsulfonyl,

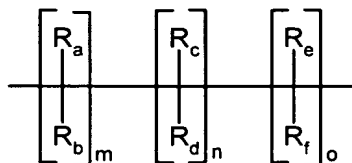
whereas, if more than one rest Z is present ($m \geq 2$), the substituents Z are equal or different from each other,

and wherein the bonds marked with an arrow are single or double bonds; or an N-oxide of said compound, wherein one or more N-atoms carry an oxygen atom, or a salt thereof, and/or a compound of ~~general~~ general formula IV

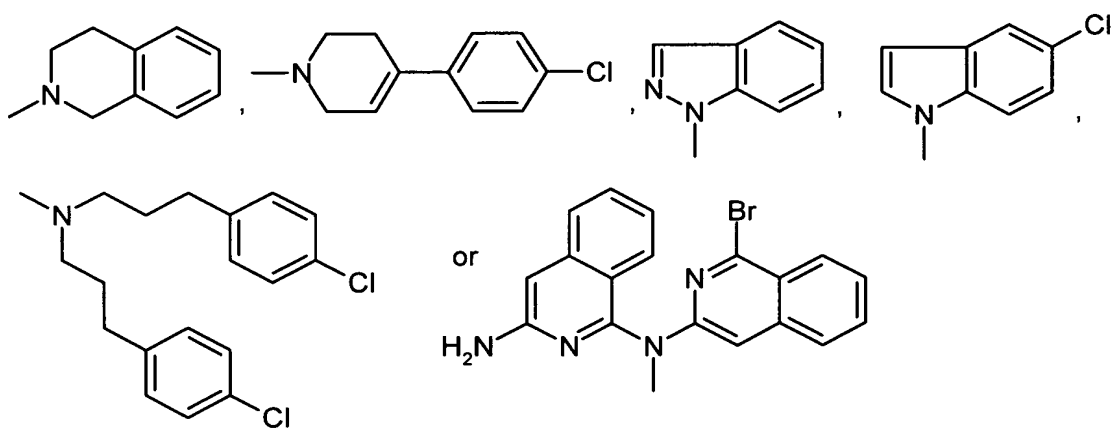


in which

A has the meaning of group $=NR^2$,
 W has the meaning of oxygen, sulfur, two hydrogen atoms or the group $=NR^8$,
 Z has the meaning of the group $=NR^{10}$ or $=N-$, $-N(R^{10})-(CH_2)_q-$, branched or unbranched C_{1-6} -Alkyl or is the group



or A, Z and R¹ together form the group



m, n and o

has the meaning of 0 – 3,

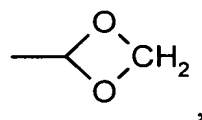
q

has the meaning of 1 – 6,

R_a, R_b, R_c, R_d, R_e, R_f

independently from each other have the meaning of hydrogen, C₁₋₄ alkyl or the group =NR¹⁰, and/ or R_a and/ or

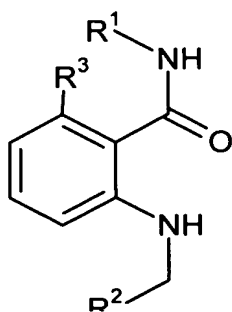
- R_b together with R_c and or R_d or R_c together with R_e and/ or R_f form a bound, or up to two of the groups R_a - R_f form a bridge with each up to 3 C-atoms with R^1 or R^2 ,
- X has the meaning of group $=NR^9$ or $=N-$,
- Y has the meaning of group $-(CH_2)_p$,
- p has the meaning of integer 1-4,
- R^1 has the meaning of unsubstituted or optionally substituted with one or more of halogene, C_{1-6} -alkyl, or C_{1-6} -alkyl or C_{1-6} -alkoxy, which is optionally substituted by one or more of halogen, or is unsubstituted or substituted aryl or heteroaryl,
- R^2 has the meaning of hydrogen or C_{1-6} -alkyl, or form a bridge with up to 3 ring atoms with R_a - R_f together with Z or R_1 ,
- R^3 has the meaning of monocyclic or bicyclic aryl or heteroaryl which is unsubstituted or optionally substituted with one or more of für halogen, C_{1-6} -alkyl, C_{1-6} -alkoxy or hydroxy,
- R^4 , R^5 , R^6 and R^7 independently from each other have the meaning of hydrogen, halogene or C_{1-6} -alkoxy, C_{1-6} -alkyl or C_{1-6} -carboxyalkyl, which are unsubstituted or optionally substituted with one or more of halogene, or R^5 and R^6 together form the group



R^8 , R^9 and R^{10} independently from each other have the meaning of hydrogen or C_{1-6} -alkyl, as well as their isomers and salts,

and/ or a compound of general formula V

V,

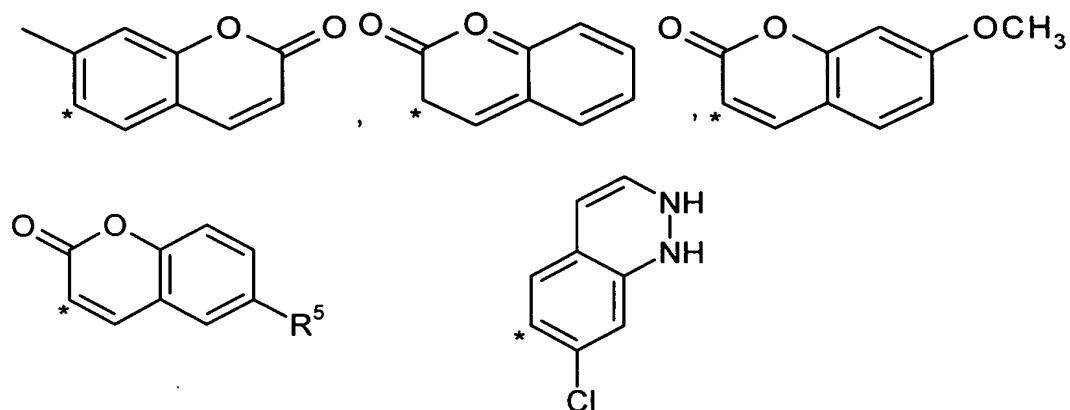


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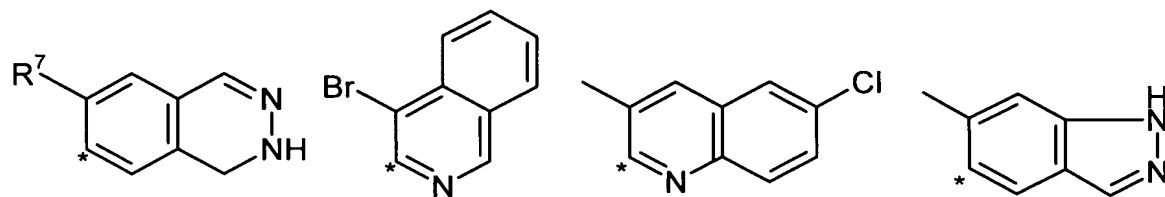
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in which

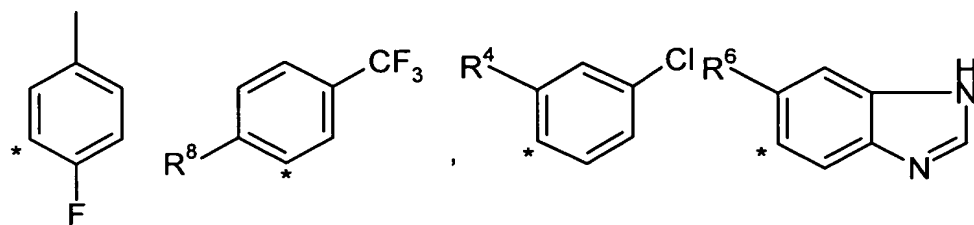
R^1 has the meaning of group



in which R^5 is chloro, bromo or the group $-OCH_3$,



in which R^7 is $-CH_3$ or chloro,

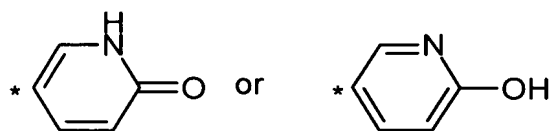


in which R⁸ is -CH₃, fluoro, chloro or -CF₃

in which R⁴ is fluoro, chloro, bromo, -CF₃, -N=C, -CH₃, -OCF₃ or -CH₂OH

in which R⁶ is -CH₃ or chloro

R² has the meaning of pyridyl or the group



and

R³ has the meaning of hydrogen or fluoro, as well as their isomers and salts.

16. (Currently Amended) Pharmaceutical compositions according to claim 15 which comprise as compound I and/or II (4-Chlorophenyl)[4-(4-pyridylmethyl)-phthalazin-1-yl]ammonium hydrogen succinate.

17. (Currently Amended) Pharmaceutical compositions according to ~~claims~~ claim 1-16 which comprise as compound I (4-Chlorophenyl)[4-(4-pyridylmethyl)-phthalazin-1-yl]ammonium hydrogen succinate, sTie2, mAB 4301-42-35, scFv-tTF and/ or L19 scFv-tTF conjugate, and as compound II (4-Chlorophenyl)[4-(4-pyridylmethyl)-phthalazin-1-yl]ammonium hydrogen succinate, sTie2, mAB 4301-42-35, scFv-tTF and/ or L19 scFv-tTF conjugate, with the provision that compound I is not identically to compound II.

18. (Currently Amended) Pharmaceutical compositions according to ~~claims~~ claim 1-17 which comprise as compound I (4-Chlorophenyl)[4-(4-pyridylmethyl)-phthalazin-1-yl]ammonium hydrogen succinate and as compound II sTie2, mAB 4301-42-35, scFv-tTF and/ or L19 scFv-tTF conjugate.

19. (Currently Amended) Pharmaceutical compositions according to ~~claims~~ claim 1-17 which comprise as compound I mAB 4301-42-35 and as compound II sTie2, and/ or scFv-tTF conjugate.

20. (Currently Amended) Pharmaceutical compositions according to ~~claims~~ claim 1-17 which comprise as compound I scFv-tTF conjugate and as compound II sTie2 and/ or mAB 4301-42-35.

21. (Currently Amended) Pharmaceutical compositions according to ~~claims~~ claim 1-17 which comprise as compound I L19 scFv-tTF conjugate and as compound II sTie2.

22. (Currently Amended) Use of pharmaceutical compositions according to ~~claims~~ claim 1-24, for the production of a medicament for the treatment of tumors, cancers, psoriasis, arthritis, such as rheumatoide arthritis, hemangioma, angiofibroma, eye diseases, such as diabetic retinopathy, neovascular glaucoma, kidney diseases, such as glomerulonephritis, diabetic nephropathie, malignant nephrosclerosis, thrombotic microangiopathic syndrome, transplantation rejections and glomerulopathy, fibrotic diseases, such as cirrhotic liver, mesangial cell proliferative diseases, arteriosclerosis, damage of nerve tissues, suppression of the ascites formation in patients and suppression of VEGF oedemas.